Vanadium and iron complexes for catalytic oxidation

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Chapter 9

Conclusions and Future Prospects

9.1 Introduction

The oxidation chemistry of vanadium(V) peroxide complexes has attracted renewed attention with the discovery in 1983 of a naturally occurring vanadium containing enzyme, vanadium bromoperoxidase.[1,2] To get a better understanding of the working mechanism of the enzyme, many vanadium(V) complexes have been prepared and studied as functional enzyme mimics. Furthermore, the coordination chemistry of vanadium related to its biological functions has been extensively explored.[3]

The tendency of vanadium(V) to coordinate peroxides was already known for decades. A classic spot test for vanadate, for instance, is the formation of the red oxoperoxovanadium(V) ion.[1] However, since only a limited number of vanadium complexes have been investigated as oxidation catalysts so far, it was our intention to develop and study a number of different types of vanadium complexes. To gain insight in the catalytic properties of these compounds, we envisioned to study the biomimetic properties of our novel complexes (*i.e.* to examine their catalytic properties in bromination reactions) and to use them as catalysts in a variety of other oxidation reactions, like epoxidations and hydroxylation reactions.

In this chapter, the results on the vanadium and iron oxidation chemistry are summarised. General conclusions will be drawn on the use of vanadium complexes as oxidation catalysts and recommendations for future research will be given.

9.2 Oxidation catalysis with high-valent vanadium complexes

As described in Chapters 3, 5, and 6, several ligands proved to be successful to incorporate vanadium.[4] The resulting complexes (Figure 9.1) were structurally characterised in detail and their oxidising properties were studied in bromination and epoxidation reactions. However, also several new ligands were synthesised (see Chapters 4 and 7), that turned out to be unsuitable for vanadium coordination, since no well-defined complexes could be isolated.

Complex **3.1** was tested whether it could serve as a functional mimic for vanadium bromoperoxidase in a reaction where trimethoxybenzene (TMB) was used as substrate and hydrogen peroxide as the oxidant. Bromination activity was indeed observed. The best result was obtained using 10 mM of TMB, 50 mM of Bu_4NBr, 10 mM of H_2O_2, and 8 mM HCl. A conversion of 62% towards TMBBr was reached in one hour (with a blank reaction of

18%). However, it was shown that the applied acidic conditions caused the dissociation of the ligand from the vanadium centre. As a result, the observed catalysis was actually accomplished by a bare vanadium(V) species. Furthermore, it was shown that simple vanadium reagents, like *e.g.* $VO(acac)_2$ are often almost as active or even more active than ligated complexes.

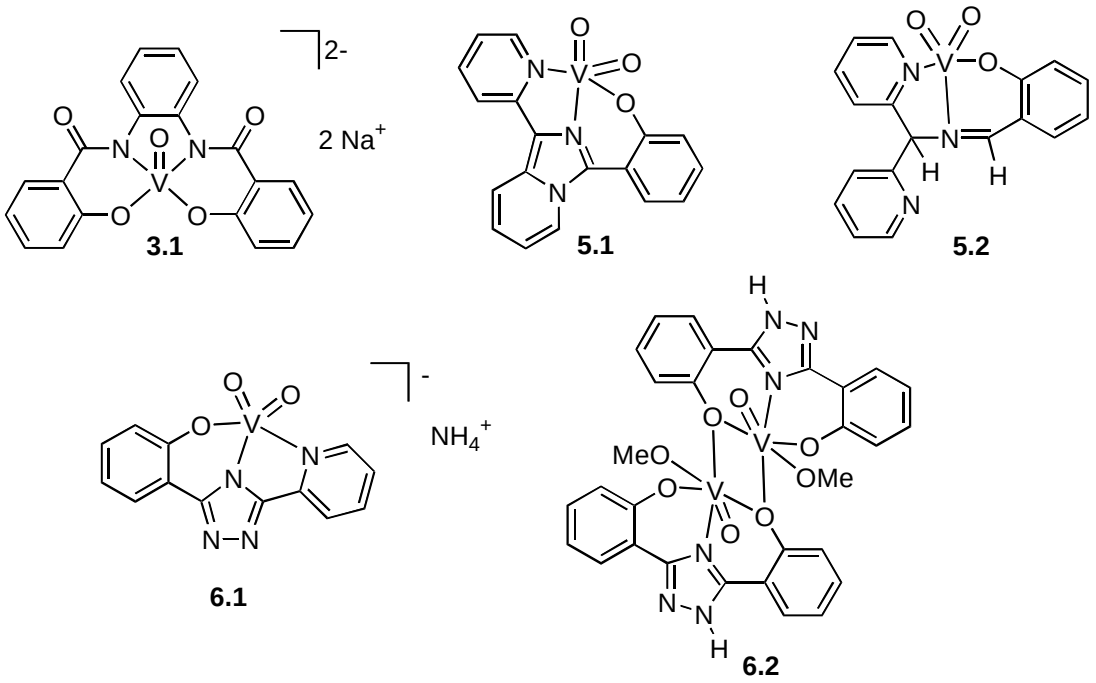

Figure 9.1 *Summary of the vanadium complexes tested as catalysts in oxidation reactions.*

The biomimetic properties of complexes **5.1** and **5.2** were also investigated. However, both complexes were catalytically inactive, since no bromination activity was observed. Complexes **6.1** and **6.2** were used as catalysts in the epoxidation reaction of cinnamyl alcohol. Although, especially for **6.2**, reasonable turnover numbers towards the epoxide were obtained, the commercially available $VO(acac)_2$ turned out to be even more active.

In Chapter 7 we focussed on the design and synthesis of new chiral ligands. Attempts were made to synthesise new chiral vanadium complexes which could subsequently be applied as catalysts in asymmetric oxidation reactions. Unfortunately, no well-defined vanadium species could be isolated. However, we were able to obtain a novel manganese complex based on a pyridine *N*-oxide salen-derived ligand, but preliminary experiments showed that this complex was inactive in the catalytic epoxidation of styrene.

9.3 Future prospects

Although predictions regarding the applicability of ligands for coordination of vanadium(IV) or vanadium(V) appear difficult to make, it seems that at least one oxygen donor atom is required for the formation of well-defined vanadium species. In general, tridentate ligands readily afford dioxovanadium(V) complexes. Tetradentate ligands are suitable for the synthesis of stable oxovanadium(IV) or -(V) complexes. The stability and robustness of the complexes is particularly put to the test in functional models for vanadium bromoperoxidase, since these complexes have to be resistant to the harsh, acidic conditions necessary for the reaction to proceed. These conditions easily cause dissociation of the ligand from the vanadium centre and therefore often two or three oxygen donor sites are needed to afford the required stability.

Bare vanadium(V) species already display high activity in bromination reactions. For example, *cis*-dioxovanadium(V) (VO_2^+) catalyses the bromination of TMB with a turnover rate of 15 mol TMBBr / mol vanadium h^{-1}.[5] Furthermore, most ligated functional model systems known in the literature only equal this activity, whereas V-BrPO functions with a turnover rate of 4.7 x 10^5 mol Br-product / mol enzyme h^{-1}. Even the best mimic known until now, developed by Butler *et al.*, appears to be only a slightly better catalyst than $VO(acac)_2$.[6] Therefore, the search for a ligand system that provides a catalyst capable of approaching the enzyme in reaction rate and selectivity remains a difficult task. Obviously, the structural environment of the vanadate in the enzyme plays an important role in the catalytic process, so the fact that the structure of the active site is now known in detail may facilitate the design of a catalyst which indeed resembles the reaction rates of the enzyme.

Vanadium-catalysed epoxidations of allylic alcohols using *tert*-butylhydroperoxide (TBHP) are well-known, since high yields are obtained and the reactions often proceed regioselective.[7] Especially commercially available $VO(acac)_2$ is very appropriate for this purpose and is therefore often recommended as the catalyst.[8] High regioselectivities are a result of coordination of the allylic alcohol to the vanadium centre. Only vanadium complexes of bidentate ligands have the required vacant coordination sites for binding of the allylic alcohol and the peroxide in an η^2 manner. To achieve different product selectivities, other ligated vanadium species could be applied as shown in Chapter 6.

A thriving topic in vanadium chemistry is the search for chiral vanadium catalysts for the asymmetric epoxidation of allylic alcohols. Many effective systems have already been developed.[9] Moderate-to-high enantioselectivities and yields were reached in the allylic epoxidation of a range of disubstituted allylic alcohols using a *N*-bis(1-naphthyl)methyl-substituted hydroxamic acid.[10] Until now, the ligands used for asymmetric allylic epoxidations are mainly bulky hydroxamic acids, which are not easily accessible. In the near future the research will therefore certainly be focussed on the development of other, more simple, bulky bidentate ligands for the synthesis of vanadium epoxidation catalysts.

In recent years many promising results have been reported in the field of vanadium catalysed asymmetric sulfide oxidations also, especially by Bolm and Ellman.[9d-f] High yields and enantioselectivities were reached with a limited number of substrates. The best results

were reported by Ellman *et al.* using a Schiff base ligand derived from *tert*-leucinol.[9d] In the asymmetric oxidation of *tert*-butyl disulfide, 98% conversion and 91% e.e. were reached. However, e.e's above 80% with simple sulfides like methyl phenyl sulfide have never been achieved. Future research in asymmetric vanadium-catalysed sulfoxidation chemistry should therefore be concentrated on the development of chiral vanadium complexes capable of oxidising a broader range of sulfide substrates.

A real challenge remains the development of a vanadium catalyst capable of epoxidation of unfunctionalised olefins, since only low turnovers can be achieved with $VO(acac)_2$. Furthermore, research regarding vanadium-catalysed oxidation of alcohols to their corresponding aldehydes and ketones as well as hydroxylation reactions has remained highly underexposed.

9.4 Oxidation catalysis with iron complexes

As described in Chapter 8, a new non-heme diiron(III) complex $[(L^1)Fe\text{-}O\text{-}Fe(L^1)](ClO_4^-)_2$ (**8.5**) (for HL^1, Figure 9.2) has been synthesised and characterised. The ligand is closely related to the well-known all-nitrogen pentadentate ligand N4Py.[11] The complex proved to be an excellent catalyst for the selective oxidation of primary and secondary alcohols using hydrogen peroxide.[12] Yields up to 65% based on H_2O_2 were reached. A remarkable increase in reaction rate was achieved by the addition of 1 equiv. of triflic acid (CF_3SO_3H).

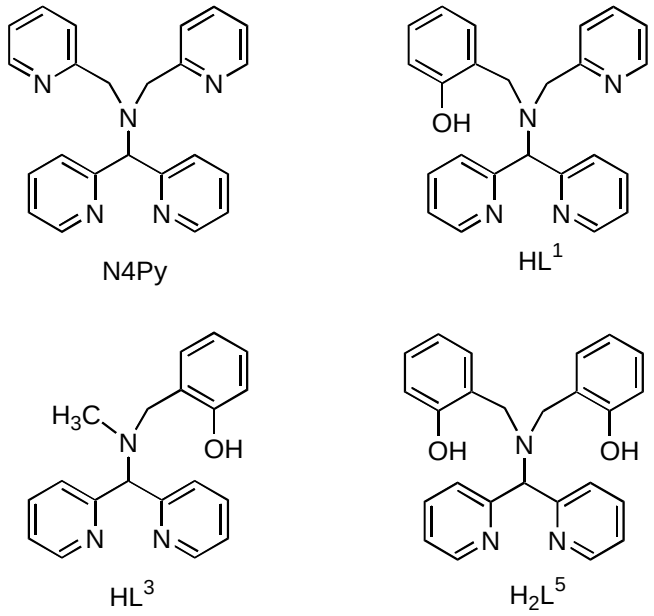

Figure 9.2 *N4Py and related ligands for iron.*

In the literature, only a few examples of iron mediated alcohol oxidations are known. For instance, the oxidation of alcohols by Fenton's reagent (Fe^{2+}-H_2O_2) has been investigated[13] as well as oxidations using potassium ferrate(VI) (K_2FeO_4),[14] but these are stoichiometric oxidation reactions.

For the N4Py-Fe system comparable turnover numbers in the catalytic oxidation of benzyl alcohol were found as for **8.5**.[11a] However, in contrast to the non-selective radical type of oxidation chemistry observed for the N4Py system, complex **8.5** turned out to be a selective oxidation catalyst. To gain insight in the reaction mechanism of oxidations catalysed by the HL^1 derived iron(III) species (**8.5**), the oxidation of benzylalcohol was monitored in time by GC and UV measurements and the kinetic deuterium isotope effect was determined. Several observations suggest that the active oxidising complex is a mononuclear species in which the phenolic moiety is no longer coordinated to the iron centre. Nevertheless, in order to reveal the exact mechanism, additional experiments with model substrates need to be done. Furthermore, spectroscopic techniques like resonance Raman, UV-Vis, or EPR spectroscopy, as well as kinetic measurements may give deeper insight in the nature of reactive intermediates and reaction pathways.

To study the effect of ligand variations on the properties of the corresponding iron species even further, additional pentadentate and tetradentate ligands related to N4Py were synthesised (HL^3, H_2L^5 in Figure 9.2). The complexation chemistry of these ligands with iron was investigated and a few complexes were isolated and characterised. On account of the promising results obtained with **8.5**, the oxidising properties of these new iron complexes deserve to be explored in detail as well.

9.5 References

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